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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SANG, HONG	
ART UNIT	PAPER NUMBER
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/784,012	SRIVASTAVA, PRAMOD K.	
	Examiner	Art Unit	
	Hong Sang	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,9,10,17,19,20,23,25-32,35 and 40-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,9,10,17,19,20,23,25-32,35 and 40-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/22/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RE: Srivastava

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/22/07 has been entered.

2. Claim 2, 9, 10, 17, 19, 20, 23, 25-32, 35 and 40-47 are pending. New claims 46 and 47 have been added. Claim 2 has been amended.

3. Claims 2, 9, 10, 17, 19, 20, 23, 25-32, 35 and 40-47 are under examination.

4. The information disclosure statement (IDS) filed on 6/22/07 has been considered. A signed copy is attached hereto.

Rejections Withdrawn

5. All previous rejections are withdrawn in view of applicant's amendment to the claims.

New Grounds of Rejections

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 2, 9, 10, 17, 19, 20, 23, 25-32, 35 and 40-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Li (US Patent No. 6,984,389, Data of Patent 1/10/2006, earliest effective filing date at least 12/16/2002), in view of the teachings of Srivastava et al. (US 2001/0034042, Pub. Date: 10/25/01, earliest effective filing date at least 1/12/2001), Srivastava (US Patent No. 6,168,793, Data of Patent 1/2/2001), and Wallen et al. (US Patent No. 5,747,332, Date of Patent: 5/15/1998).

Li teaches a method of treating cancer in a subject, and a method for improving the treatment outcome in a subject in need of treatment for cancer comprising (a) administering to the subject a sub-optimal amount of a purified alpha-2-macroglobulin preparation comprising a population of non-covalent alpha-2-maroglobulin-pepide complexes obtained from cancerous tissue of the subject; and (b) administering to the subject at least one treatment mortality, wherein the alpha-2-marcoglobulin preparation can be administered concurrently, before, or after the administration of the treatment modality, wherein the treatment modality include chemotherapeutic agents (see column 6, lines 16-40) and the subject is a human (see column 13, line 46). Li teaches that that antigenic peptides and/or components can be eluted from HSP/α2M complexes either in the presence of ATP or low pH, and once isolated, they can be purified and complexed

in vitro to HSP or α2M to form the HSP or α2M complexes of the invention (see column 42, lines 46-67, and column 43). Li teaches that the α2M complexes can also be prepared by mixing α2M-polypeptide and antigenic molecules in the presence of a protease (see column 48, lines 33-67). Li teaches that such α2M-peptide complexes are preferably autologous to the individual subject, i.e., obtained from the tissues of the subject receiving the administration of α2M-peptide preparation and treatment modality (see column 8, lines 18-23), and the autologous α2M-peptide complexes can be isolated from a metastasis tumor (see column 12, lines 18-21). Li teaches that the α2M preparation and the therapeutic modality are administered in a sub-optimal amount (see column 29, lines 13-15, and column 52, lines 41-54). Li teaches treating tumors that are non-responsive to chemotherapy/cytokine treatment (see column 31, lines 38-42). Li teaches intradermal and subcutaneous administration of α2M-peptide preparation (see column 51, lines 12-21). Li teaches that the α2M-peptide complexes can be administered weekly for about 4-6 weeks (see column 50, lines 46-49) and the preparation can be administered to the same or different sites (see column 30, lines 9-10). Li teaches α2M complexes wherein the peptide is covalently and non-covalently bond to α2M (see column 12, lines 1-2). Li teaches digestion of peptides with protease (see column 48, lines 57-58). Li teaches using exogeneous antigenic molecules for making α2M complexes (see column 44, lines 41). Specifically, Li teaches that the peptides either isolated by the procedures taught in the specification or chemically synthesized or recombinantly produced may be reconstituted with a variety of purified natural or recombinant stress proteins in vitro to generate immunogenic non-covalent

stress protein-antigenic molecules complexes (see column 46, lines 20-29). Li teaches that the identity of the antigenic molecules of the α2M peptide-complexes need not be known (see column 42, lines 37-40). Li further teaches that exogenous antigen or antigenic or immunogenic fragments or derivatives thereof can be complexed to stress proteins (see column 46, lines 29-31). Li et al. teaches that α2M preparation may include crude cell lysate comprising α2M , and the amount of lysate corresponding to between 100-10^8 cell equivalents (see column 12, lines 24-27).

Li does not teach subjecting said protein preparation to cleavage by the one or more non-enzymatic methods, wherein the cleavage is cyanogens bromide cleavage. Li does not teach one or more adjuvants, wherein the adjuvant is selected from the group consisting of QS-21, monophosphoryl lipid A, muramyl dipeptide, threonyl-muramyl dipeptide, a glucosamine disaccharide, and Leishmania elongation factor. Li does not specifically teach a protein preparation that comprises total cellular proteins, total cytosolic protein, total membrane-bound protein, or total protein in a cellular fraction of cells of said type of cancer, wherein said cellular fraction is selected from the group consisting of a membrane fraction and an organelle fraction, wherein the organelle fraction is a nuclear, mitochondrial, lysosomal or endoplasmic reticulum-derived fraction. However, these deficiencies are made up for in the teachings of Srivastava (10/25/01), Srivastava (1/2/01) and Wallen et al.

Srivastava (10/25/01) teaches that HPBF-antigenic complexes may optionally be administered with one or more adjuvants in order to enhance the immunogenic response, wherein the adjuvants can be muramyl dipeptide, monophosphoryl lipid A,

polyphosphazene (see paragraph [0325]). Srivastava teaches peptide-binding HSP fragments may be obtained by chemical or enzymatic (protease) cleavage of native or recombinant HSPs, wherein the specific chemical cleavage can be performed by cyanogen bromide (see paragraph [0192]).

Srivastava (1/2/01) teaches a method of treating a mammal having a tumor comprising administering a therapeutically effective amount of a purified population of non-covalent heat shock protein 70-peptide complexes to a first mammal having a tumor, wherein said population comprises a plurality of different non-covalent heat shock protein 70-peptide complexes, each of said different complexes containing a different peptide, and wherein said population of non-covalent heat shock protein 70-peptide complexes is isolated from tumor tissue of the same type as said tumor of a second mammal, wherein the first mammal and send mammal are the same (see claims 39-41). Srivastava teaches the immunogenic composition of the invention are ideal vaccination because the hsp 70-peptide complex has a number of different peptides associated with it, which potentially may include a number of different antigens capable of binding to a variety of epitopes and are capable of binding the entire spectrum of antigenic peptides regardless of the MHC haplotype of a given cells (see column 5, lines 25-50).

Wallen et al. teach that a HSP complex can be produced by mixing an already purified heat shock protein with a cell lysate, a membrane isolate (materials isolated from a cell membrane), or a protease treated cell lysate containing peptides, polypeptides, denatured proteins (see column 2, lines 58-62).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Li to include one or more adjuvants in the composition and to digest a cell lysate or a membrane isolate with a protease such as cyanogens bromide in view of the teachings of Srivastava (10/25/01), Srivastava (1/2/01), and Wallen et al. One would have been motivated to do so because Srivastava (10/25/01) teaches that adjuvants enhances the immunogenic response and non-enzymatic agent such as cyanogens bromide works as well as protease. Moreover, Srivastava (1/2/01) teaches the complexes that comprise a population of HSP complexes are capable of binding the entire spectrum of antigenic peptides in a tumor cell, and as such they would be more effective than a composition of which comprises only one or three HSP complexes. One of ordinary skill in the art would have a reasonable expectation of success to do so because Srivastava (10/25/01) teaches a method of treating a cancer using an hsp composition comprising one or more adjuvants and Srivastava (10/25/01) teaches digestion of hsp complexes with cyanogens bromide. Moreover, using protease treated cell lysate or membrane isolate to make heat shock protein-antigenic peptides complex is known in the art as shown by Wallen. Li demonstrates that α2M works in a way that is very similar to heat shock proteins by presenting the tumor antigenic peptides to the immune cells. Li et al. teaches a method of treating cancer using α2M preparation that includes crude cell lysate (see column 12, lines 24-27).

Because the claim 46 recites the term "comprises" which is open, a cell lysate of Wallen et al. would comprise the total protein in an organelle fraction.

8. Claims 2, 9, 10, 17, 19, 20, 23, 25-33, 35, and 40-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Armen (WO 02/11669A2, 2/14/2002) in view of Srivastava et al. (US 2001/0034042, Pub. Date: 10/25/01, earliest effective filing date at least 1/12/2001), Srivastava (US Patent No. 6,168,793, Data of Patent 1/2/2001), and Wallen et al. (US Patent No. 5,747,332, Date of Patent: 5/15/1998).

Armen teaches a method of treating a primary and metastatic cancer in a subject comprising administering a composition to said subject, wherein the composition comprises an α2M, a saponin and an antigenic molecule, the antigenic molecule displays the antigenicity of an antigen of a cancerous cell, the antigenic molecule can be covalently or noncovalently bound to the α2M (see abstract, and page 14, lines 7-8), and the subject is a human (see page 74, line 21). Armen teaches the composition of the invention can comprise three antigenic molecules (see page 13, lines 10-14). Armen teaches that the composition of the invention can be administered alone or in combination with one or more chemotherapeutic agents, wherein the chemotherapeutic agent is administered prior or subsequent to administration of composition comprising α2M preparation (see page 73, lines 16-34). Armen teaches that the α2M, and/or antigenic molecules are preferably autologous to the individual, and can be isolated as naturally-occurring complexes from cancer cells or can be chemically synthesized or recombinantly produced (see page 15, lines 3-7). Armen teaches that the α2M/antigenic peptide complexes can be prepared in the presence of a proteinase (see page 22, lines 34-36 and page 23). Armen teaches that the antigenic peptides can be isolated by using ATP or low pH reagents such as trifluoroacetic acid (TFA) (see page

31). Armen teaches that the composition of the invention can be administered intradermally or subcutaneously once weekly for about 4-6 weeks (see page 68, line 30), wherein the same site can be repeated after a gap of one or more injections (see page 74, lines 1-12). Armen teaches that the immunogenic composition of the invention comprises sub-immunogenic amounts of its individual components (see page 75, lines 1-9). Armen teaches that antigenic molecule refers to a peptide or other molecule with which hsps are endogenously associated in vivo (e.g. in cancerous tissue), as well as exogenous antigens/immonogens (i.e. with which the hsps are not complexed in vivo) or antigenic/immunogenic fragments and derivatives thereof (see page 14, lines 24-28). Armen teaches such exogenous antigens and fragments and derivatives thereof for use in complexing with hsp or α2M can be selected from among those known in the art (see page 14, lines 28-30). Armen teaches alpha-2-marcoglobulin preparation comprising an adjuvant such as saponin or XS-21 (see page 14, lines 17-19 and line 32). Because the instant claims use the word "comprising" which is open language, the composition recited in the instant claims does not exclude other agents such as saponin used in Armen's composition.

Armen does not teach subjecting the protein preparation to cleavage by the one or more non-enzymatic methods, wherein the cleavage is cyanogens bromide cleavage Armen does not specifically teach a protein preparation that comprises total cellular proteins, total cytosolic protein, total membrane-bound protein, or total protein in a cellular fraction of cells of said type of cancer, wherein said cellular fraction is selected from the group consisting of a membrane fraction and an organelle fraction, wherein the

organelle fraction is a nuclear, mitochondrial, lysosomal or endoplasmic reticulum-derived fraction. However, these deficiencies are made up for in the teachings of Srivastava (10/25/01), Srivastava (1/2/01) and Wallen et al..

Srivastava (10/25/01) teaches that HPBF-antigenic complexes may optionally be administered with one or more adjuvants in order to enhance the immunogenic response, wherein the adjuvants can be muramyl dipeptide, monophosphoryl lipid A, polyphosphazene (see paragraph [0325]). Srivastava teaches peptide-binding HSP fragments may be obtained by chemical or enzymatic (protease) cleavage of native or recombinant HSPs, wherein the specific chemical cleavage can be performed by cyanogen bromide (see paragraph [0192]).

Srivastava (1/2/01) teaches a method of treating a mammal having a tumor comprising administering a therapeutically effective amount of a purified population of non-covalent heat shock protein 70-peptide complexes to a first mammal having a tumor, wherein said population comprises a plurality of different non-covalent heat shock protein 70-peptide complexes, each of said different complexes containing a different peptide, and wherein said population of non-covalent heat shock protein 70-peptide complexes is isolated from tumor tissue of the same type as said tumor of a second mammal, wherein the first mammal and send mammal are the same (see claims 39-41). Srivastava teaches the immunogenic composition of the invention are ideal vaccination because the hsp 70-peptide complex has a number of different peptides associated with it, which potentially may include a number of different antigens capable of binding to a variety of epitopes and are capable of binding the entire

spectrum of antigenic peptides regardless of the MHC haplotype of a given cells (see column 5, lines 25-50). Because the Hsp70-peptide complexes of Srivastava are isolated from a tumor cell lysate (see example 5), thus such complexes include a mixture of all Hsp70-peptides that may be presented in the tumor cell. Srivastava teaches immunogenic composition comprising one or more adjuvants, such as muramyl dipeptide, and QS-21 (see column 4, lines 9-14).

Wallen et al. teach that a HSP complex can be produced by mixing an already purified heat shock protein with a cell lysate, a membrane isolate (materials isolated from a cell membrane), or a protease treated cell lysate containing peptides, polypeptides, denatured proteins (see column 2, lines 58-62).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Armen to use a composition comprising a population of α2M complexes, such as the one that is prepared by complexing α2M to protease treated cell lysate or membrane isolate, to treat a metastatic cancer in view of the teachings of Srivastava (10/25/01), Srivastava (1/2/01), and Wallen. One would have been motivated to do so because Srivastava teaches the complexes that comprise a population of HSP complexes are capable of binding the entire spectrum of antigenic peptides in a tumor cell, and as such they would be more effective than a composition of which comprises only one or three HSP complexes. Moreover, one of ordinary skill in the art would have a reasonable expectation of success to modify the method of Armen to use a composition comprising a population of α2M complexes, such as the one that is prepared by complexing α2M to protease

treated cell lysate or membrane isolate, to treat a metastatic cancer because Srivastava (1/2/01) teaches a method of making a composition comprising a population of hsp70-peptide complex and Srivastava (1/2/01) was successful on treating cancer using such composition, Armen teaches a method of treating cancer using a complex comprising three hsp-peptide complexes or three α2M-peptide complexes, and moreover, Armen demonstrates that α2M works in a way that is very similar to heat shock proteins by presenting the tumor antigenic peptides to the immune cells. Furthermore, using protease treated cell lysate or membrane isolate to make heat shock protein-antigenic peptides complex is known in the art as shown by Wallen.

Because the claim 46 recites the term "comprises", a cell lysate of Wallen et al. would comprise the total protein in an organelle fraction.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 2, 9, 10, 17, 19, 20, 23, 25-32, 35, 40-43, 46 and 47 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 48-50 of U.S. Patent No. 6,984,389, in view of the teachings of Armen (WO 02/11669A2, 2/14/2002), and Wallen et al. (US Patent No. 5,747,332, Date of Patent: 5/15/1998).

Claims 48-50 of US Patent No.6,984,389 are drawn to a method for treating cancer in a subject, a method for improving the treatment outcome in a subject in need of treatment for cancer comprising the steps of:

(a) administering to said subject a sub-optimal amount of a purified alpha-2-macroglobulin preparation comprising a population of alpha-2-macroglobulin-peptide complexes that (i) display the antigenicity of a tumor-specific antigen or tumor-associated antigen of said type of cancer or (ii) are isolated from cancerous tissue of said subject; and

(b) subsequenct to step (a), administering to said subject at least one treatment modality in an amount effective for treatment of said cancer; wherein said at least one treatment modality comprises a tyrosine kinase inhibitor; wherein in the absence of step (b), said sub-optimal amount is ineffective for treatment of said cancer and wherein in the absence of step (a), said cancer does not respond to said treatment modalities.

Claims 48-50 of US Patent No.6,984,389 do not teach one or more adjuvants. Claims 48-50 of US Patent No.6,984,389 do not teach that the population of complexes

is produced by exposing the protein preparation to protease, wherein the protein preparation comprises total cellular proteins, total cytosolic protein, total membrane-bound protein, or total protein in a cellular fraction of cells of said type of cancer, wherein said cellular fraction is selected from the group consisting of a membrane fraction and an organelle fraction, wherein the organelle fraction is a nuclear, mitochondrial, lysosomal or endoplasmic reticulum-derived fraction. Claims 48-50 of US Patent No.6,984,389 do not teach intradermal or subcutaneously administration of the composition to the same site of the subject at weekly intervals. However, these deficiencies are made up for in the teachings of Armen and Wallen et al.

Armen teaches that the α2M/antigenic peptide complexes can be prepared in the presence of a proteinase (see page 22, lines 34-36 and page 23). Armen teaches that the antigenic peptides can be isolated by using ATP or low pH reagents such as trifluoroacetic acid (TFA) (see page 31). Armen teaches that the composition of the invention can be administered intradermally or subcutaneously once weekly for about 4-6 weeks (see page 68, line 30), wherein the same site can be repeated after a gap of one or more injections (see page 74, lines 1-12). Armen teaches α2M complexes wherein the peptide may be covalently and non-covalently bond to α2M (see page 13, lines 10-14). Armen teaches the alpha-2-marcoglobulin preparation can be administered concurrently with chemotherapy (see page 73, lines 28-29). Armen teaches digestion of peptides with protease (see (see page 22, lines 34-36 and page 23). Armen teaches alpha-2-marcoglobulin preparation comprising an adjuvant such as saponin or XS-21 (see page 14, lines 17-19 and line 32).

Wallen et al. teach that a HSP complex can be produced by mixing an already purified heat shock protein with a cell lysate, a membrane isolate (materials isolated from a cell membrane), or a protease treated cell lysate containing peptides, polypeptides, denatured proteins (see column 2, lines 58-62).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made and one would have been motivated to modify the method of claims 48-50 of U.S. Patent No. 6,984,389 to use the protease treated cell lysate or membrane isolate to make a population of alpha-2-macroglobulin-peptide complexes and administer the composition intradermally or subcutaneously to the same site of the subject once weekly to treat cancer in view of the teachings of Armen and Wallen et al. because the complexes that comprise protease treated cell lysate are capable of binding the entire spectrum of antigenic peptides in a tumor cell, and as such they would be more effective. Moreover, one of ordinary skill in the art would have a reasonable expectation of success to administer the composition intradermally or subcutaneously to the same site of the subject once weekly to treat cancer because such methods are well known in the art as taught by Armen. Furthermore, using protease treated cell lysate or membrane isolate to make heat shock protein-antigenic peptides complex is known in the art as shown by Wallen.

Because the tyrosine kinase inhibitor is one type of at least one treatment modality, the teachings of claims 48-50 of US Patent No. 6,984,389 anticipate this specific limitation i.e. at least one treatment modality. Because the claim 46 recites the

term "comprises", a cell lysate of Wallen et al. would comprise the total protein in an organelle fraction.

Claim 1-3, 15, 17, 19, 20, 23, 25-33, 35, 40-43, 46 and 47are directed to an invention not patentably distinct from claims 48-50 of commonly assigned US Patent No. 6,984,389 for the reasons set forth above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned US Patent No. 6,984,389, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

11. Claims 2, 9, 10, 17, 19, 20, 23, 25-33, 35, 40-43, 46 and 47 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2-4 and 8 of copending Application No. 10/546,106 in view of in view of the teachings of Armen (WO 02/11669A2, 2/14/2002), and Wallen et al. (US Patent No. 5,747,332, Date of Patent: 5/15/1998).

Claims 2-4 and 8 of copending Application No. 10/546,106 are drawn to a method for treating a cancer in a patient comprising the steps of a) isolating a complex of α2M from a bodily fluid of a mammal having said cancer; and b) administering an amount of said isolated complex effective to treat said cancer in said patient, wherein the complex is a population of complexes of α2M bound to different antigenic molecules in which the different antigenic molecules comprise on which has the antigenicity of an antigen specific to said cancer, the antigenic molecule is derived from a tumor, the method further comprising, prior to or at the same time as step b), the step of administering a chemotherapeutic agent to said patient. Because the complex of α2M is isolated from a bodily fluid and is a population of complexes of α2M, such population would include all the mixtures of α2M complexes presented in a bodily fluid.

Claims 2-4 and 8 of copending Application No. 10/546,106 do not teach one or more adjuvants. Claims 2-4 and 8 of copending Application No. 10/546,106 do not teach that the population of complexes are produced by exposing the protein preparation to protease, and complexing the population of antigenic peptides to α2M, wherein the protein preparation comprises total cellular proteins, total cytosolic protein, total membrane-bound protein, or total protein in a cellular fraction of cells of said type

of cancer, wherein said cellular fraction is selected from the group consisting of a membrane fraction and an organelle fraction, wherein the organelle fraction is a nuclear, mitochondrial, lysosomal or endoplasmic reticulum-derived fraction . However, these deficiencies are made up for in the teachings of Armen and Wallen et al.

Armen teaches that the α2M/antigenic peptide complexes can be isolated as naturally-occurring complexes from cancer cells or can be chemically synthesized or recombinantly produced (see page 15, lines 3-7). Armen teaches that the α2M/antigenic peptide complexes can be prepared in the presence of a proteinase (see page 22, lines 34-36 and page 23). Armen teaches that the antigenic peptides can be isolated by using ATP or low pH reagents such as trifluoroacetic acid (TFA) (see page 31), then complexed to α2M. Armen teaches α2M complexes wherein the peptide may be covalently and non-covalently bond to α2M (see page 13, lines 10-14). Armen teaches the alpha-2-marcoglobulin preparation can be administered concurrently with chemotherapy (see page 73, lines 28-29). Armen teaches digestion of peptides with protease (see (see page 22, lines 34-36 and page 23). Armen teaches alpha-2-marcoglobulin preparation comprising an adjuvant such as saponin or XS-21 (see page 14, lines 17-19 and line 32).

Wallen et al. teach that a HSP complex can be produced by mixing an already purified heat shock protein with a cell lysate, a membrane isolate (materials isolated from a cell membrane), or a protease treated cell lysate containing peptides, polypeptides, denatured proteins (see column 2, lines 58-62).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made and one would have been motivated to modify the method of claims 2-4 and 8 of copending Application No. 10/546,106 to use the protease treated lysate or membrane isolate to prepare the α2M complexes because the complexes that comprise protease treated cell lysate are capable of binding the entire spectrum of antigenic peptides in a tumor cell, and as such they would be more effective. Moreover, one of ordinary skill in the art would have a reasonable expectation of success to prepare the composition using protease treated cell lysate or membrane isolate because such methods are well known in the art as shown by the teachings of Wallen et al. Because the claim 46 recites the term "comprises", a cell lysate of Wallen et al. would comprise the total protein in an organelle fraction.

Claim 1-3, 19, 20, 23, 25, 32, 33, 35, 40-43, 46 and 47 are directed to an invention not patentably distinct from claims 2-4 and 8 of commonly assigned copending Application No. 10/546,106 for the reasons set forth above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned copending Application No. 10/546,106, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions

were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Conclusion

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Sang whose telephone number is (571) 272 8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Hong Sang
Art Unit 1643
Oct. 24, 2007

/Christopher Yaen/
Primary Examiner
Art Unit 1643
October 25,2007